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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,135	10/18/2006	Amar Lulla	PAC/23225 US (4137-00600)	8688

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EXAMINER	
WESTERBERG, NISSA M	

ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,135	LULLA ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 - 34, 53* is/are pending in the application.

4a) Of the above claim(s) *4 - 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 - 3, 11 - 34, 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 9, 2009 has been entered.

2. Applicants' arguments, filed November 9, 2009, have been fully considered but they are not deemed to be fully persuasive. The following rejections and/or objections constitute the complete set presently being applied to the instant application.

Response to Amendment

3. The declaration under 37 CFR 1.132 filed November 9, 2009 is insufficient to overcome the rejection of the pending claims based upon Jasprova (WO 02/03963), Flash-Ner-Barak et al. (WO 02/00204) or Katdare et al. (WO 95/29679) as set forth in the last Office action because: the only evidence presented in the declaration is in regards to the compositions of the instant application and only presents an opinion by

one of the inventors regarding the compositions which are disclosed in the applied prior art.

Claim Rejections - 35 USC § 112 – 2nd Paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 34 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is MAINTAINED for the reasons of record set forth in the Office Actions mailed September 24, 2008 and May 8, 2009 and those set forth below.

Applicant traverses this rejection on the grounds that the term "substantially free" is familiar to one of ordinary skill in the art and is necessarily defined by the context of the specification. Paragraph [0008] is referenced and as the degradation products are inactive, Applicants have defined an upper limit and the term has a lower limit of zero.

These arguments are unpersuasive. The referenced paragraph merely states that the degradation products result in a brown color, are inactive and this degradation process is enhanced by water. This in no way indicates the amounts of these products that would be considered substantial and therefore fall outside the scope of the instant claims. Depending on the circumstances, a majority componet (e.g., >50%) could be considered to make something present in a substantial amount or a much smaller

amount of a toxic or undesirable product could be considered a substantial amount. The Examiner agrees that the lower limit is zero, but without guidance as to what level of degradation products and/or inactivated active ingredient is considered a "substantial" amount, the rejection is maintained.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1 – 3, 11 – 22, 25 – 32, 34 and 53 were rejected under 35 U.S.C. 102(b) as being anticipated by Jasprova et al. (WO 02/03963). This rejection is MAINTAINED for the reasons of record set forth in the Office Actions mailed September 24, 2008 and May 8, 2009 and those set forth below.

Applicant traverse this rejection on the grounds that claim 35 was rejected as being anticipated by this piece art. As the limitations from claim 35 have been incorporated into independent claims 1 and 14, the pending claims are not anticipated.

This argument is unpersuasive. Claim 35 contained limitations regarding the process by which the oral formulation was prepared. Independent claims 1 and 14 are now product-by-process claims."[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a

different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) **MPEP 2113**.

Neither the declaration by Geena Malhotra nor the arguments of Applicant provide evidence that the process of dry blending with an aqueous binder as recited in the instant claims and the direct compression process used by Jasprova result in different product. Therefore, the rejection is maintained.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1 – 3, 11 – 22, 25 – 32, 34 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jasprova (WO 02/03963).

Jasprova discloses a tablet obtained by direct compression of alendronic acid or its pharmaceutically acceptable salts, a diluent, a dry binder, a disintegrating agent and a lubricant wherein the diluent is a combination of at two diluents except lactose (p 8, ¶ 3). Lactose is known to interact with sodium alendronate, especially in the presence of water, to hasten its degradation (p 2, ¶ 3). The at least two diluents except for lactose comprise 20 – 80% by weight of the tablet of microcrystalline or pulverized cellulose or calcium hydrogenphosphate and 0.001 to 50% by weight of mannitol (a carbohydrate alcohol), modified starches and phosphates or hydrogenphosphate or alkali or alkaline earth metals (p 8, ¶4). A preferred composition is 10 – 50% by weight mannitol and 30 – 70% by weight microcrystalline cellulose (MCC; p 9, ¶3). However, a modified starch together with mannitol also results in a product with appropriate quality (p 10, ¶ 3). In formulations 3A – 3D (p 13, ¶ 6 - p 14), compositions including about 8.5% starch by weight are prepared, about 10% by weight bisphosphonic acid compound, varying amounts of mannitol (65%, 30%, 20% and 10%) and granulated MCC (15%, 50%, 60%

and 70%) and 1% by weight of the lubricant/glidant magnesium stearate is used. Jasprova also discloses that formulations alendronic acid salts can be manufactured using a wet granulation process (p 2, ¶ 3). While wet or dry granulation is an extra step in the manufacturing process, such a step makes possible the compression of mixture that could otherwise not be tabletted (p 2, ¶ 3).

Jasprova does not prepare a composition using a wet granulation process in which a dry blend of bisphosphonic acid derivative and carbohydrate alcohol is wet granulated with an aqueous binder.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to prepare a bisphosphonic acid derivative and carbohydrate alcohol by a wet granulation process. The person of ordinary skill in the art would have been motivated to make those modifications and reasonably would have expected success because Japsrova discloses that wet or granulation are suitable methods by which formulations can be prepared.

Shown on p 17 of Jasprova are data regarding the stability over time for the various formulations indicating that at 3 and 6 months, the amount of active ingredient in the tablets was the same as when first prepared, indicating a lack of formation of degradation products as required in claim 34.

11. Claims 1 – 3, 11 – 34 and 53 were rejected under 35 U.S.C. 103(a) as being unpatentable over Jasprova (WO 02/03963) in view of Flash-Ner-Barak et al. (WO

02/00204). This rejection is MAINTAINED for the reasons of record set forth in the Office Actions mailed September 24, 2008 and May 8, 2009 and those set forth below.

12. Claims 1 – 3, 11 – 34 and 52 were rejected under 35 U.S.C. 103(a) as being unpatentable over Jasprova and Flash-Ner-Barak et al. further in view of Katdare et al. (WO 95/29679). This rejection is MAINTAINED for the reasons of record set forth in the Office Actions mailed September 24, 2008 and May 8, 2009 and those set forth below.

Applicant traverses these rejections on the grounds that the prima facie case of obviousness must fail because of a showing of unexpected results. As set forth in the declaration of Geena Malhouta, the instantly claimed process produces bisphosphonic acid formulations that are stable for up to 24 months under the indicated storage conditions. Flash-Ner-Barak and Katdare are silent as to stability of their formulations and the formulations of Jasprova disclose stability data over a 6 month time frame and do not provide information as to the water content of the formulation, a factor which is known to one of ordinary skill in the art to be directly related to the stability of the formulation.

These arguments are unpersuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the water content of the formulation) are not recited in the rejected claim(s). Although the claims are interpreted in light of the

specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In order to overcome a *prima facie* case of obviousness, it is incumbent upon the Applicant to provide comparative test evidence that demonstrates unexpected superiority of the claimed compositions versus the closest prior art compositions, and not simply an advantage predictable from the prior art. See *In re Chapman*, 148 USPQ 711, 715 (CCPA, 1966). As noted previously, the declaration does not contain any evidence regarding the formulations of the cited prior art, only those of the instant application. The comparison necessary to establish unexpected results must be a side by side comparison carried out by Applicants to show that the difference is truly unexpected and not a difference in factors such as the person performing the experiment and/or equipment and ingredients used. Therefore, in order to overcome the prima facie case of obviousness with the secondary consideration of unexpected results, applicants must run and compare the stability of their particular claimed formulations to the stability of the formulations of the cited prior art.

Moreover, such proffered comparisons must be commensurate in scope with the breadth of the claims. See *In re Clemens*, 206 USPQ 289, 296 (CCPA, 1980) and *In re Coleman*, 205 USPQ 1172, 1175 (CCPA 1980). The declaration provides stability data for two different storage conditions. However, it is unclear what formulation(s) these data relate to as three different examples are presented in the specification. The data must be sufficient to establish the unexpected results for the full scope of the claims. This means that unexpected results must be established for different bisphosphonic

acid derivatives and different carbohydrate alcohols in a range of amounts. As the formulations that provide the reported stability have not be identified and the various examples in the specification all use mannitol as the carbohydrate alcohol, the offered comparison are not commensurate in scope with the breadth of the claims. While the stability of all formulations and ingredients need not be provided, sufficient data must be presented so that a trend can be established (see MPEP 716.02(d)).

It is also noted that Katdare et al. explicitly discloses the use of a wet granulation process in the preparation of the (e.g., example 1, p 11). Thus, it is known in the art that formulations of these ingredients can be prepared by a wet granulation process (Katdare) or can be compressed into tablets without granulation (Jasprova). One of ordinary skill in the art would select the appropriate methodology for the preparation of the composition based on the equipment available, the compression characteristics of the material without a granulation step and based on the other manufacturing requirements.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jake M. Vu/
Primary Examiner, Art Unit 1618

NMW